A more detailed experience with the measurement of specific urinary marker proteins has recently been published [4].

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Reply from the authors

This letter from Regeniter et al about the best method to correctly assess the selectivity of proteinuria is rather confusing. In one instance, they compare the selectivity index with the IgG/transferrin ratio, while in Table 1 and another text mention the selectivity index is compared with the transferrin/IgG ratio. Moreover, the authors do not specify whether the patients they studied had nephrotic proteinuria. The very high rates of unselective proteinuria reported in Table 1, very different from the rates usually found in patients with nephrotic syndrome from primary glomerulonephritis, suggest that most patients tested had low levels of proteinuria. It is well known that in this case the value of the selectivity index is not reliable.

In our study [1] we measured IgG and transferrin by immunonephelometry in second-morning urine samples (**Methods** section) and calculated the selectivity index according to the formula of Cameron and Blandford [2] in 89 patients with nephrotic syndrome. The simple calculation of the IgG/transferrin ratio in the same 89 patients shows values very different from that obtained by the usual formula (Table 1). Moreover, our classification of the selectivity index in patients with nephrotic syndrome and baseline normal renal function fits very well with the functional outcome: remission, high selectivity (HS) 100%; moderate selectivity (MS) 50%; and nonselectivity (NS) 29%; $P = 0.0001$ and progression to chronic renal failure, HS 0%, MS 25%, and NS 35%; $P = 0.05$. The selectivity index calculated as urinary IgG/transferrin ratio does not show this type of association. Furthermore, our results in patients with focal segmental glomerulosclerosis and minimal change disease are similar to the results of Laurent et al [3], who found that 100% of patients with a selectivity index ≤ 0.07 were steroid-responsive, while all patients with a selectivity index ≥ 0.17 were steroid-resistant. Finally, if, according to the suggestion of Regeniter et al, urinary α_2-macroglobulin is measured, they are measuring three proteins, while we are measuring four proteins (serum and urinary IgG and transferrin). That is not a very big and "laborious" difference!

Table 1. Glomerular selectivity assessed by selectivity index vs. urinary IgG/transferrin ratio

	N	SI	IgG/transferrin
SI $\leq$ 0.10 (HS)	15	0.07 ± 0.02	0.24 ± 0.11
SI $\geq$ 0.11 $\leq$ 0.20 (MS)	34	0.15 ± 0.03	0.50 ± 0.25
SI $\geq$ 0.21 (NS)	40	0.33 ± 0.11	1.17 ± 1.19

Abbreviations are: HS, high selectivity; MS, moderate selectivity; NS, nonselectivity; SI, selectivity index according to the formula of Cameron and Blandford [2]; IgG/transferrin, ratio of IgG over transferrin measured in second morning urine samples.

In conclusion, in our opinion, the selectivity index is clinically useful in patients with nephrotic syndrome and the correct method to assess the selectivity of proteinuria is by using the formula of Cameron and Blandford [2].

Another method used to evaluate the characteristics of both the glomerular and tubular components of proteinuria is to measure, in second morning urine samples, some proteins with different molecular weight [for example, IgG 150 kD and α_1-microglobulin (α_1m) 31.8 kD] expressed in milligrams per gram of urinary creatinine (U_{Cr}). In patients with membranous nephropathy (abstract; Bazzi et al, *J Am Soc Nephrol* 9, 84A, 1998, updated and submitted for publication) we found that the patients with IgG excretion $<$ vs $\geq$ 110 mg/g U_{Cr} have 100% and 20% remission ($P = 0.0001$), respectively, and the patients with α_1m excretion $<$ vs $\geq$ 33.5 mg/g U_{Cr} have 0% vs. 58% progression to chronic renal failure ($P = 0.0001$), respectively.

This is the most simple method to evaluate the quality of proteinuria because only two urinary proteins are measured and their levels that, respectively, reflect the alteration of size-selectivity and the impairment of tubular reabsorption of microproteins, have a high predictive value of functional outcome, at least in patients with idiopathic membranous nephropathy.

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Cited "validation" references for the SphygmoCor device

To the Editor: Covic et al describe attempts to measure "central arterial pressure waveforms" in hemodialysis patients in Romania [1]. They claim their noninvasive assessments of "aortic" blood pressure (BP) waveforms using the SphygmoCor device (PWV Medical, Inc., Sydney, Australia) have been validated. However, they cite no data to support this assertion.

The authors write, "The software analytical program also derived in real time from the measured radial artery waveform an aortic BP waveform using a validated transfer function algorithm" [1, p 2636]. However, this is not correct. The two references cited (23 and 24) have nothing to do with the SphygmoCor and have not validated the SphygmoCor's generalized transfer function (GTF) algorithm.

Reference 23 is a 2-page short report from a 1992 Supplement, a year before both the SphygmoCor radial artery GTF was published [2], and the technique's United States Patent was granted [3]. Reference 24 did not use the SphygmoCor, but rather involved another GTF developed using a completely different computational technique. This approach has subsequently been shown to be ineffective in 67% of cases, when calibrated noninvasively [4].

A search on Medline reveals a paucity of validation work with the SphygmoCor reported in the literature. Furthermore, no evidence has been provided to support the use of the device in patients with renal failure, let alone in those following hemodialysis. Given this, researchers may wish to exercise caution in making claims about the "validity" of the noninvasive approach, which, at present, remains completely unproven, especially in renal disease.

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Reply from the author

We thank Dr. Eldon Lehmann for his letter and the interest he has shown in our recent publication [1].

Over the last 2 years Dr. Lehmann, a noted expert in vascular imaging and methodology, with a long-standing interest in arterial compliance, has repeatedly censured other authors of other studies in which similar methods have been used [2–4].

Interested readers are urged to follow this correspondence trail across time, and several journals, the better to appreciate the background to these comments.

The thrust of his comments to us can be summarized as follows. First, is there any justification/supportive evidence for the use of a reverse generalized energy transfer function (GTF), as opposed to an individualized energy transfer function? Second, which parameters can safely be derived using a validated-GTF? Third, has there been any independent validation of the use of such GTFs with noninvasively calibrated brachial artery blood pressure? Finally, have the methodology and algorithms in use in the SphygmoCor device (PWV Medical, Inc., Sydney, Australia) been validated? Our answers (for brevity) are, "yes; aortic systolic blood pressure and augmentation index; yes, but not yet in the public domain; and partly." We have reason to hope that later this year the answer to all of the questions will be "yes." Until then, we concede that complete validation of this extremely interesting and potentially useful pulse wave analysis technique is (eagerly) awaited.

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